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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,922	08/05/2002	Albert B. Deisseroth	044574-5059-US	6375

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EXAMINER	
PRIEBE, SCOTT DAVID	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 02/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,922	DEISSEROTH, ALBERT B.	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *5 and 11-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-10,29 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 May 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20030609,20030630*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement filed 6/9/03 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein as WO 95/21259 has not been considered.

Furthermore, the 1449A/PTO filed with the information disclosure statements of both 6/9/03 and 6/30/03 do not comply with 37 CFR 1.98(b)(5), which requires that identification of the publications (non-patent literature) include the title of the publication in addition to the author, place of publication (journal), volume-issue numbers, page numbers and date. See MPEP 609, III.A.(1). The non-patent publications listed on the 1449A/PTO forms have been considered, but the listed non-patent publications have not been initialed. The publications will not be printed on the face of a patent unless Applicant provides a PTO-1449 (or acceptable substitute) that is fully compliant with 37 CFR 1.98. It is noted that the Leavitt and Lin publications listed on the 1449A/PTO filed 6/30/03 are also listed on the 1449A/PTO filed 6/9/03. It is noted that the publication date is incorrect in the Berkner citation (6/9/03 form).

The reference in the first sentence of the specification to Disclosure Document 441607 filed 8/7/98 is noted. However, it is unclear whether Applicant fulfilled the requirements of the

Disclosure Document program by filing of a separate letter referring to DD 441607 in a patent application within two years of 8/7/98. See MPEP 1706.

Election/Restrictions

Claims 5 and 11-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/30/04. The subject matter of elected group I is a conditionally replication competent adenovirus (CRAD) wherein the adenovirus comprises an E1A region under control of a plastin promoter, i.e. the E1A gene meets the limitation of a gene whose induction modifies the metabolism of a cell.

Drawings

The drawings are objected to because Figures 3B1 & 3B2 are too dark to discern any detail. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement

Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 1-4, 10, 29 and 30 objected to because of the following informalities. The claims embrace non-elected inventions, and should be amended to reflect the election.

Appropriate correction is required in reply to this Office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6-10, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hallenbeck et al., WO 96/17053 in view of both Park (Cancer Res. 54: 1775-1781, 1994) and Leavitt, WO 94/17182 alone or both in combination with Mueller et al., US 6,383,785 and Koerner et al., US 6,033,856.

The elected invention is directed to a conditionally replicating adenovirus (CRAD) vector that replicates in neoplastic cells but not in normal epithelial cells, wherein the adenoviral E1A region is placed under the control of the L-plastin promoter.

Hallenbeck et al. discloses CRAD vectors for the treatment of tumors *in vivo* and pharmaceutical compositions comprising them. The CRAD comprises a tumor specific promoter operably linked to an adenoviral gene required for replication of the adenovirus, linkage to the adenoviral E1 region is preferred. The promoter used is active in tumor tissue, but not significantly in normal tissue. Expression from the tumor specific promoter leads to replication of the CRAD selectively in tumor cells and leads to lysis of the tumor cells and infection of additional tumor cells. Little or no replication of the CRAD occurs in non-target tissue, which then avoid the cytolytic consequences of the adenovirus. See entire reference, especially pages 6-11; page 14, line 27 to page 15, line 19; page 17; page 20, lines 27-30; pages 21-22; page 25, lines 18-27 and claims 1-40. Hallenbeck teaches several different tumor specific promoters to be used in the CRAD vectors for treating different types of cancer, but does not teach using the L-plastin promoter in a CRAD.

However, Park (page 1775) and Leavitt (pages 1-3) disclosed that the promoter of the L-plastin gene is a strong, constitutively-expressed, tissue-specific promoter in a wide variety of carcinomas and sarcomas, primarily of epithelial origin, particularly in mammary, ovarian, and chorio carcinomas. However, normal tissues and cells, its expression is limited to cells of hematopoietic origin, e.g. leukocytes; it is not expressed in normal epithelial tissue. Expression of L-plastin in non-hematopoietic tissue is considered to be indication of cancer. Leavitt describes vectors comprising the L-plastin promoter region from about 5 kb upstream to 111 bp

downstream of the transcription start site for expression of structural genes only in cells that express L-plastin, such as cancer cells. In particular, the structural gene may encode a product that is toxic to cancer cells, and the vector may then be used to specifically kill cancer cells. See Leavitt at page 13, lines 1-12; pages 15-17, and 20-22.

In addition, Koerner and Mueller disclose constructs designed to direct expression of a desired product in a cell-specific manner for treatment of diseases. Briefly, the inventions disclosed in these patents relate to a positive-feedback expression system where a cell-specific promoter directs expression of a transcription factor, and a promoter responsive to the transcription factor directs expression of a therapeutic product. Treatment of tumors is one of the disclosed uses of the inventions, and both teach the use of the L-plastin promoter as the cell-specific promoter to use for treatment of ovarian and pancreatic tumors. See Koerner especially at col. 5, line 36 to col. 6, line 19; col. 14, lines 33-44; *col. 17, lines 7-19; and col. 18, line 31 to col. 20, line 67, and Mueller especially at col. 5, lines 29-48; col. 6, lines 20-33; col. 6, line 55 to col. 7, line 27; col. 16, lines 18-33; *col. 20, lines 23-38; col. 22-24.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the L-plastin promoter into a CRAD of Hallenbeck, operably linked to the E1 region for example in order to limit replication of the CRAD to specific types of tumors. Hallenbeck taught that for targeting tumor cells, a tumor specific promoter was required that would be not be significantly expressed in non-target cells. Park and Leavitt disclosed that the L-plastin promoter directed expression of genes linked to it in a wide variety of tumor types, and directed expression in normal cells only of hematopoietic origin. Leavitt also disclosed taking advantage of this restricted expression to direct expression of a

toxin in tumor cells for the purpose of selectively killing them. In addition, Koerner and Mueller taught the use of the L-plastin promoter to direct tumor-specific expression of therapeutic proteins in ovarian and pancreatic tumors. One of skill in the art would have recognized from the disclosures of Park and Leavitt, and additionally from Koerner and Mueller, that the L-plastin promoter could be used to target expression to specific tumor cells, and that consequently, the L-plastin promoter was suitable for use in the CRAD of Hallenbeck, such as for treatment of mammary or ovarian carcinomas or pancreatic tumors.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe
Primary Examiner
Art Unit 1632